Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action mailed March 19, 2003 (the "Office Action"). Claims 20-40 are pending in the present application. Claims 20-40 stand rejected under 35 U.S.C. § 102, and under 35 U.S.C. § 103. The concerns raised by the Examiner are addressed below.

I. Interview Summary

Applicant's representative, Shawna Cannon Lemon, appreciated the opportunity to speak with Examiners Micah-Paul Young and Carlos Azpuru on May 30, 2003 regarding the present application. Applicant appreciates the Examiner's willingness to consider this Amendment in view of discussions directed to α-dihydroergocryptine and bromocriptine as the active compounds of the formulations of the present invention.

II. Claim Rejection Under 35 U.S.C. § 102

Claims 20-23, 25-28, 30-38 and 40 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,069, 911 to Züger ("Züger"). Applicant respectfully traverses this rejection.

The Office Action states the following:

> Züger teaches a sustained release combination of ergot derivatives such as α-dihydroergocryptine (col. 1, lin. 55-60) with hydrophilic swelling agents and pharmaceutical excipients such as hydroxypropylcellulose and beeswax (col. 2, lin. 30-55). The reference teaches a ratio of ergot derivative to hydrophilic swelling agent of 1:0.5 to 1:2 (col. 2, lin. 57-58). The reference also teaches that α-dihydroergocryptine is present in the formulation concentrations from 4.5 to 7.5 mg (examples). These disclosures render the claims anticipated.

Office Action, page 2.

Applicant directs the Examiner's attention to column 2, lines 57-58 of Züger. In contrast to the assertions of the Office Action, Züger proposes that it is the "ratio of hydrocolloid to other excipent" that may be from 1:0.5 to 1:2. Column 2, lines 57-58 (emphasis added). Züger does not teach that ratio of ergot derivative to hydrophilic swelling agent is from 1:0.5 to 1:2 as stated in the Office Action. Moreover, Züger proposes that preferred ratios of 9,10-dihydro ergot alkaloid to swelling substance are from about 1:4 to 1:50 (Col. 4, lines 44-45), preferably the ratio of co-dergocrine to

swelling substance is from 1:50 to 1:10 (Col. 4, lines, 52-53), and preferably the ratio of dihydroergotamine to swelling substance is from 1:4 to 1:20 (Col. 4, lines 66-67). Thus, Züger clearly does not teach a ratio of ergot derivative to hydrophilic swelling agent of 1:0.5 to 1:2 as recited in the claims of the present invention.

Applicant further directs the Examiner's attention to the examples set forth in Züger. In contrast to the assertions of the Office Action, the examples set forth in Züger propose that co-dergocrine (generic name of a molar 3:3:2:1 mixture of dihydroergocornine, dihydroergocristine, dihydro-α-ergocryptine and dihydro-β-ergocryptine) and dihydroergotamine are present in the formulation concentrations from 4.5 to 7.5 mg. Formulation concentrations of α-dihydroergocryptine are not provided, and thus, do not provide an adequate disclosure for a formulation directed to α-dihydroergocryptine as recited in the claims of the present invention.

Applicant has also added new claims 41-51 that further recite aspects of the present invention that are not disclosed by Züger. For example, new claim 47 recites as follows:

> 47. (new) A sustained-release pharmaceutical composition comprising:
>
> about 5 to about 80 mg α-dihydroergocryptine;
>
> a pharmaceutically acceptable swelling agent or mixture thereof, wherein the ratio of α-dihydroergocryptine to swelling agent is about 1:0.5 to about 1:10; and
>
> one or more pharmaceutically acceptable excipients;
>
> said composition having a bioavailability at least equal to the bioavailability of α-dihydroergocryptine administered using a conventional drug delivery system.

Thus, upon further consideration of Züger, it becomes apparent that the propositions relied upon by the Office Action have been misinterpreted. For at least these reasons, the "disclosures" as stated above in the Office Action are not, in fact, disclosures and do not render the present claims anticipated by Züger.

Accordingly, Applicant respectfully submits that claims 20-23, 25-28, 30-38 and 40 are patentable under 35 U.S.C. § 102(b), and respectfully requests that this rejection be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 24, 29 and 39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Züger in view of U.S. Patent No. 3,752,888 to Fluckiger et al. (Fluckiger et al.). Applicant respectfully traverses this rejection.

The Office Action states that "[a]s discussed above Züger teaches elements of the claimed invention. What is lacking is a teaching of bromocriptine as the ergot derivative. Fluckiger et al. teaches a brominated ergocryptine product, which can be combined with hydrophilic swelling agents and other excipients." Office Action, page 3, citations omitted. The Office Action further states that "[a] skilled artisan would have been motivated to substitute the compounds of Fluckiger into the formulation of Züger in order to impart alternative therapeutic properties on the formulation." Office Action, page 3.

As noted above, Züger does not teach the present invention. The mere substitution of the compounds of Fluckiger into the formulation of Züger would not provide the present invention. Moreover, the initial motivation to combine these references is lacking where Züger is directed to 9,10 dihydrogenated ergot alkaloid containing compositions and Fluckiger is directed to 2-bromo-α-ergocryptine as a lactation inhibitor. For at least these reasons, Applicant respectfully submits that claims 24, 29 and 39 are not obvious over Züger in view of Fluckiger.

Applicant does not believe that a *prima facie* case of obviousness has been established by the Office Action. As a precautionary measure, however, Applicant resubmits herewith a Declaration Under 37 C.F.R. § 1.132 of Dr. Federico Mailland (the "Mailland Declaration"). The Mailland Declaration was previously submitted in response to the 35 U.S.C. § 103(a) obviousness rejection (and not a § 102 rejection) as set forth in the Office Action mailed April 3, 2002 in which the Office Action specifically stated the following:

> The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, **the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences** (emphasis added).

Office Action of April 3, 2002, page 5.

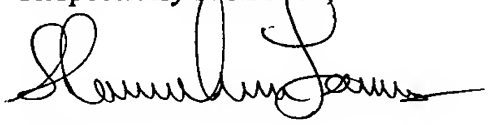
In general, the Mailland Declaration clearly shows that ergot derivative formulations of the present invention provide greatly improved bioavailability in comparison to conventional formulations as well as in comparison to ergot derivative formulations prepared according to Züger. Thus, Applicant respectfully submits that the products and methods of the present invention are structurally and functionally distinct from the product and method proposed by Züger.

Accordingly, Applicant respectfully submits that claims 24, 29 and 39 are patentable under 35 U.S.C. § 103(a), and respectfully requests that this rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned; who may be reached at (919) 854-1400.

Respectfully submitted,



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Susan E. Freedman
Date of Signature: September 17, 2003